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A COMPREHENSIVE REVIEW ON FORMULATION, CHARACTERIZATION EVALUATION OF PHARMACOSOMES

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ABSTRACT

Novel vesicular drug delivery devices called pharmacosomes are used. They provide a potential substitute for traditional vesicles. The amphiphilic phospholipid complexes of medicines with active hydrogen that bind to phospholipids are known as pharmacosomes. Pharmacosomes, like other vesicular systems, offer an effective way to transport medication directly to the infection site, reducing drug toxicity without causing any negative side effects. Additionally, they lower the cost of treatment by increasing drug bioavailability, particularly in the case of poorly soluble medicines. This strategy as a medication delivery system unquestionably guarantees a dependable, secure, targeted, and exact drug delivery mechanism. In addition to lowering therapy costs, drug leakage and toxicity, increasing the bioavailability of poorly soluble medications, and having restorative benefits, they aid in the regulated release of pharmaceuticals at the site of action. They are often made by hand-shaking and injecting ether. Different aspects of the pharmacosomes, such as size, surface shape, and in vitro release rate, have been assessed. This article examines pharmacosomes' potential as targeted, regulated drug delivery systems and emphasizes their manufacturing and characterization processes.

KEYWORDS: Amphiphilic, Pharmacosomes, biosomes, targeted drug delivery system, phospholipids, bioavailability.

1. INTRODUCTION

Over the past few decades, numerous researchers have been trying to further create innovative drug delivery systems. On the basis of the therapeutic benefits of these systems and their financial features, the primary reason for developing innovative drug delivery systems may be described.[1] The ideal innovative drug delivery system should meet two requirements: first, it should route the active ingredient to the intended site of action at a rate determined by the body's needs.[2] Encasing pharmaceuticals in submicroscopic drug carriers such liposomes, transferosomes, niosomes, polymeric nanoparticles, serum proteins, immunoglobulins, microspheres, erythrocytes, reverse micelles, monoclonal antibodies, and pharmacosomes is one method to alter the original biodistribution of medications.[3] Lipid vesicles have gained significance in recent years in the fields of immunology, membrane biology, diagnostic procedures, and most recently genetic engineering.[4] Vesicular structures are a type of system that extends the time that a medication is in the bloodstream and reduces toxicity by selective absorption.[5] Vesicles are colloidal particles with a water-filled core and a bilayer-arrangement wall of lipids and surfactants (amphiphiles). These amphiphiles have the ability to produce one or more concentric bilayers if the water content is raised. While liphophilic medications become stuck in the bilayered wall by electrostatic and/or hydrophobic forces, hydrophilic pharmaceuticals find a place in the interior aqueous environment.[6] Because of their propensity for oxidative breakdown and the purity of their native phospholipids, transferosomes have several limitations that are solved by pharmacosomes.[6] They work well to meet therapeutic objectives such medication targeting and controlled release. The interaction of lipids with drugs on their surface and in their bulk determines how vesicular pharmacosomes evolve. Any medication that contains an active hydrogen atom (-COOH, -OH, -NH2, etc.) can be esterified to a lipid with or without a spacer chain to produce an amphiphilic molecule.[7]

Table 1: Applications and limitations of Pharmacosomes.

S.No	Advantages	Disadvantages
1.	Drugs that are both lipophilic and hydrophilic can be included in pharmacosomes.	The amphiphilic character of a molecule affects how it is synthesised.
2.	The phase transition temperature of pharmacosomes has a substantial impact on their interactions with members in the vesicular and miceller state	Lipids and medications must interact on the surface and in the bulk.
3.	Predetermined and high drug loading	Covalent bonding is necessary to prevent medication leakage.
4.	Amphiphilicity improves the bioavailability of	Fusion, agglomeration, and chemical

	medications that are weakly lipid and water soluble.	hydrolysis occur during storage.
5.	Size, functional groups (drug molecule), chain length (lipids), and spacer determine how quickly a drug molecule degrades into an active form.	Lipids and medications must interact on the surface and in the bulk.
6.	There is a decrease in toxicity and negative consequences	To prevent medication leakage, covalent bonding is necessary.
7.	There is reduction cost of therapy	Fusion and aggregation occur during storage, in addition to chemical hydrolysis.

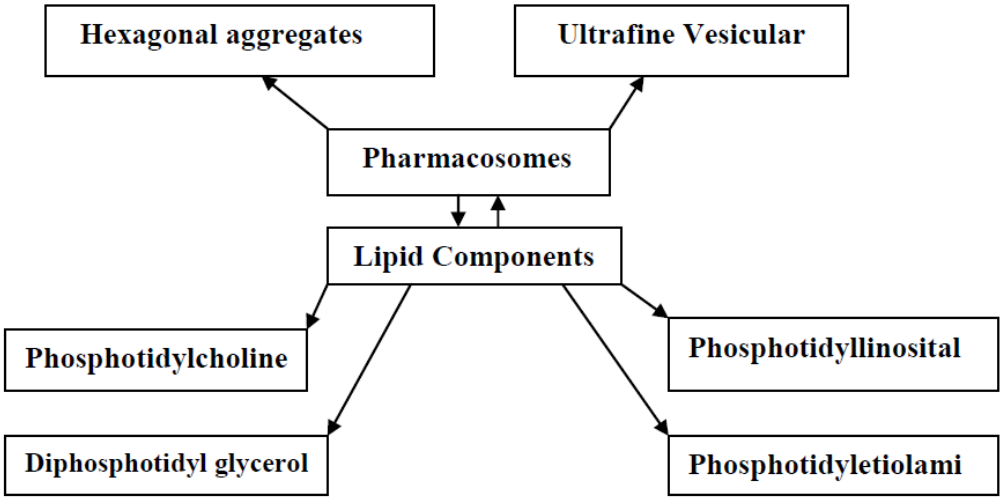

Fig 1: an emerging novel vesicular drug delivery system.

1.1.Formulation aspects of pharmacosomes

1) **Drug:** Any medication that contains an active hydrogen atom (-COOH, -OH, -NH2, etc.) can be esterified to a lipid with or without a spacer chain to produce an amphiphilic compound complexes. These artificial amphiphilic compounds facilitate membrane, tissue, or cell (pharmacosomes) transfer of walls inside an organism.[9]

2) **Lipids**

The main molecular components of cell membranes are phospholipids. Phosphoglycerides and spingolipids are the two types of phospholipids that are often employed. The phosphotidyl choline molecule is the most prevalent phospholipid.[10]

3) **Solvent**

In the creation of pharmacosomes, an analytical-grade, intermediate-polarity organic solvent is utilized. High purity and volatility are required. The medication must be dissolved together

with the phospholipids in the chosen solvent. The polarity of the medication and the lipid determine the choice of solvent.[11]

1.2 Methods of preparation

1. **Ether injection method**
2. **Solvent evaporation method / Hand shaking method**
3. **Anhydrous co-solvent lyophilization method**
4. **Supercritical fluid process**

1. Ether injection method

This technique involves appropriately mixing a drug-lipid complex solution before gently injecting it through a gauze needle into a heated aqueous media. Vesicles quickly develop as a result.

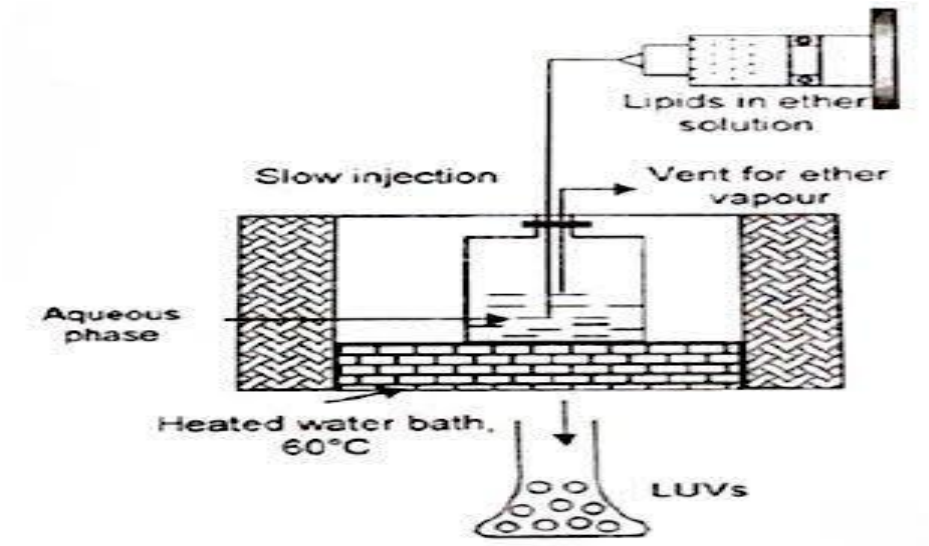

Fig 2. ether injection method.

2. Solvent evaporation method / Hand shaking method

In a flask with a flat bottom, a combination of lipid, drug, and various excipients is dissolved in an organic solvent such di-ethyl ether. By gently shaking a round bottom flask under low pressure at room temperature, or by employing a rotating evaporator, ether is extracted. The dry film is gently stirred and hydrated with aqueous phase at 50–60 °C to create multilamellar vesicles (MLVs) with a large diameter.[12]

3. Anhydrous co-solvent lyophilization method

Drugs and phospholipids are first dissolved in a dimethyl sulfoxide solution containing glacial acetic acid. After stirring the mixture to get a clear liquid, it is overnight freeze-dried at condenser temperature. The resulting complex is nitrogen flushed and kept at 4°C.

4. Supercritical fluid process

Solution improved dispersion by complicated supercritical fluid is the name of this technique. In a supercritical fluid containing carbon dioxide, the drug and lipid complex are first premixed, and then high super saturation is attained by passing through the nozzle mixture chamber.

The rapid mixing of the dispersion caused by the turbulent flow of the solvent and carbon dioxide leads in the creation of pharmacosomes.

5. Recent approaches

- A hydrophobic medication called Adriamycin was combined with a polymer made of polyxyethylene glycol and polyaspartic acid to create a biodegradable micelle-forming drug combination.
- Diluting the micelle without causing the monomeric drug conjugate's active ingredient to precipitate. Muller-Goymann and Hamann's experiment with diluting lyotropic liquid crystals of an amphiphilic substance.[13]
- By encasing amoxicilin, phosphotidylethanolamine with varied phosphotidylecholine and cholesterol molar ratios greatly improved cytoprotection. Using aqueous domain, Singh et al. created vesicular structures.[14]

1.3. Evaluation of Pharmacosomes

2. Complex Determination

The correlation spectrum is used The FTIR spectrum may be used to check the discrete elements and their mixtures as well as the production of both conjugate and complex.[15]

3. Surface Morphology

The surface morphology can be seen using scanning electron microscopy (SEM) or transmission electron microscopy (TEM). Purity grades of phospholipid have an impact on the process factors, such as rotational speed, vacuum used, or technique, as well as the form and size of pharmacosomes.

4. Drug content

The complex equivalent to the drug is weighed and placed into a volumetric flask with the appropriate solvent in order to ascertain the amount of drug in the drug-pc complex. A magnetic stirrer is used to mix the solution. The amount of medication present is assessed UV spectrophotometrically following a 24-hour suitable dilution.[16]

5. Differential scanning calorimetry (DSC)

The compatibility or interactions between the medicine and excipients are assessed using this thermal analytical approach. The disappearance of endothermic peaks, appearance of peaks, changes in peak form and start, peak temperature/melting point, and relative peak area or enthalpy are all signs that an interaction has occurred.

6. X-ray power diffraction (XRPD)

The relative integrated intensity of reflection peak is used to determine the degree of crystallinity. The area under curves of the XRPD patterns, which determine the integrated intensity, provide the specimen characteristics.

7. Fourier transform infrared spectroscopy (FTIR)

By comparing the spectrum of the complex with the spectrum of the constituent components and their mechanical mixing, IR spectroscopy may be used to validate the complex's creation**.**

8. In – vitro Study

The reverse dialysis bag technique is used to evaluate the in vitro medication release rate. Pharmacosomes are inserted into the dialysis bag using this technique, and the receiver phase is positioned outside. Each dialysis bag is withdrawn, and the contents are examined for drug release. Dialysis bags holding the continuous phase are suspended in a vessel containing the donor phase and agitated at regular intervals. The increased membrane surface area that is accessible for transfer from the donor to receptor compartment is a benefit of this method. The greater staffing efficiency provided by this method as a result of the fewer stages is another benefit.[17]

1.4. Approaches of Pharmacosomes

1) A broader stability profile and longer shelf life are provided by pharmacosomes.
2) Many researchers have employed this strategy with success to enhance the therapeutic effectiveness of numerous drugs.

3) Pharmacosomes are more selective when acting on particular target cells.[18]
4) Raikhman et al. defined pharmacosomes as building blocks capable of carrying physiologically active molecules, such as proteins and nucleic acids.[19]
5) In a research, Yi-Guang et al. created acyclovir pharmacosomes and found that the blood's plasma proteins absorbed the pharmacosomes and interfered with how erythrocytes interacted, reducing the amount of hemolysis that occurred.[20]

Table 2: Therapeutic applications of Pharmacosomes.

Drugs	Therapeutic applications
Pindolol diglyceride	Three to five fold increase in plasma concentration with lower renal clearance as compared with free drug
Amoxicillin	Improved cytoprotection and treatment of H. pylori infections in male rats
Taxol, Cytarbine,	Improved anticancer and biological activity of anticancer agents
Bupranolol hydrochloride	Enhanced effect on intraocular pressure and enhance lymph transport

CONCLUSION

There are several limitations to vesicular drug delivery methods, and pharmacosomes, like other vesicular systems, are crucial to the selection targeting, and the controlled delivery of various drugs. Pharmacosomes have immense potential, and advantages over other vesicular systems. More work has to be put into understanding the non-bilayer phases and the mechanism of action for the system. Pharmacosomes not only have a high entrapment efficiency, but also allow for planned administration because the medication itself produces vesicles when it conjugates with lipids. Pharmacosomes have a huge potential, thus additional research on this system is necessary to provide more beneficial outcomes.

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